REMARKS

Claims 1-13 and 15-71 are pending. All claims have been amended to substituted the phrase "a mecamylamine or a mecamylamine stereoisomer" for "partial nicotine agonist." This amendment is supported throughout Applicants' specification, *e.g.,* in the original claims. Further, claims 2, 7, and 10 have been amended to recite "dimethylamino mecamylamine. This amendment is supported throughout Applicants' specification, *e.g.,* at page 10, lines 15-16. Accordingly, no new matter has been added.

Rejections under 35 U.S.C. §112 are Rendered Moot

Claims 2, 7, 10, 52, 70, and 71 were rejected as allegedly indefinite based on their previous recitation of the term "mecamylamine analog." Final Office Action at page 4-5. Based on the foregoing amendment, this rejection has been rendered moot.

While Applicants' do not acquiesce regarding the alleged basis for the rejection, all occurrences of the term "mecamylamine analog" have been deleted from the currently pending claims in order to expedite prosecution in the current application. Based on the foregoing amendment, Applicants respectfully assert that the rejection is now moot and should be withdrawn.

Rejections under 35 U.S.C. §103 are Traversed

Claims 1-13 and 15-71 were rejected as allegedly unpatentably over Crooks in view Suzuki. Based on the following remarks, Applicants respectfully traverse the rejection.

All of Applicants' pending claims recite "a mecamylamine or a mecamylamine stereoisomer." No "nicotine antagonists" are claimed. Accordingly, the presently claimed aspect of the disclosed invention relates to "a mecamylamine or a mecamylamine stereoisomer," and not to nicotine antagonists generally. Further, although mecamylamine is characterized in the art as a "nicotine antagonist," it also can exhibit agonist or partial agonist properties (as discussed in additional detail below, and in Applicants' specification).

As previously noted, Crooks discussed the compounds disclosed therein as a "new class" of nicotine antagonists. See Crooks at col. 6, line 26; and at col. 13, line 56. Further, Crooks stated that "[t]he inventors show the molecules described are binding to the antagonist site in

their unprotonated forms and that the binding mode involves interaction of the quaternary ammonium nitrogen with the anionic site of the receptor." Crooks at col. 12, lines 55-58. Thus, Crooks taught a very particular class or group of compounds for the methods discussed therein, not nicotine antagonists generally. However, it should be noted that, assuming for the sake of argument only that *any* general antagonist activity is taught by Crooks, no partial agonism is taught or suggested.

Further, the lack of consideration of mecamylamine by Crooks despite the inclusion of that compound as a comparative example would have provided no motivation for one of skill in the art to examine mecamylamine as a possible compound for treatment of any of the disorders disclosed by Crooks. In fact, the use of mecamylamine as a comparative example without any consideration by Crooks of that compound for use in the methods discussed would have discouraged the skilled artisan from any use of mecamylamine in such methods. It should be noted that Crooks teaching actually comments on the distinction between the nicotine antagonists taught as part of Crooks' invention and mecamylamine, *e.g.*, in Table 3; and at col. 9, line 61 through col. 10, line 2, stating that:

> In addition, the classical competitive and noncompetitive nicotinic antagonists, DHBE (Vidal and Changeux, 1989; Alkondon and Albuquerque 1991; Mulle et al. 1991) and mecamylamine (Grenhoff and Svensson, 1989; Mulle et al. 1991) were also examined in this assay for the sake of comparison. None of the compounds examined, including DHBE and mecamylmine, had any significant effect on [^{3} H]DA release in the concentration range of 1-10 μM.

In the above-quoted passage, the comparison noted is between *mecamylamine* and *claimed compounds of the invention according to Crooks*. Accordingly, the disclosure of Crooks actually *taught away* from the presently claimed invention. Any asserted motivation to use mecamylamine according to the present invention based on Crooks' teaching regarding the antagonists discussed therein would have been fully negated by Crooks' disclosure as quoted and discussed above.

Suzuki added nothing to counter this teaching away, in that Suzuki only disclosed the classic antagonist activity of mecamylamine in the nicotine withdrawal experiments discussed therein. Suzuki provided no teaching regarding effects of mecamylamine itself (*i.e.*, as disclosed in Applicants' specification), but, rather, illustrated only the well-characterized antagonism of nicotine by mecamylamine under the particular conditions of the experiments described therein.

The experiments disclosed in Suzuki (designed to show mecamylamine-precipitated nicotine-withdrawal aversion in rats) would have provided no motivation for one of ordinary skill in the art to obtain Applicants' claimed methods, based on Applicants' discovery of a partial agonist effect of mecamylamine. No combination of teachings by Crooks and Suzuki would have provided the presently claimed invention, and, as noted, Crooks actually taught away from the use of mecamylamine in the presently claimed methods.

For at least the reason that no combination of Crooks and Suzuki taught or suggested any methods for treatment of the presently recited disorders using mecamylamine, none of Applicants' claims would be considered obvious by one of ordinary skill in the art in view of those references. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Conclusion

Applicants believe that the Application is now in condition for immediate allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned at (336) 721-3681 regarding any question concerning this filing.

Respectfully submitted,

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